PATENT SPECIFICATION

629,419

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COMPLETE SPECIFICATION

Improvements in and relating to Surgical Dressings

We, JOHNSON & JOHNSON (GREAT BRITAIN) LIMITED, a Company organised under the laws of Great Britain, of Slough, Bucks, do hereby declare the nature of this invention and in what manner the same is to be performed, to be particularly described and ascertained in and by the following statement:—

This invention relates to surgical dressings having improved hemostatic properties and concerns an improvement in or modification of the invention described in the parent Specification No. 1136/47 (Serial No. 621,230) whose characteristic feature is a hemostatic surgical dressing comprising alginic acid preferably in the fibrous state.

Surgical dressings of the type used for topical application have long been prepared by securing absorbent material such as cotton gauze to adhesive plaster, such that the gauze can be placed over a wound and the adhesive arranged to hold it in place. More recently the gauze has been treated with antiseptic or antibacterial materials, such as mercurochrome and sulphur drugs.

It has been the ordinary practice to use a bandage to cover a wound to aid the stoppage of bleeding and for the smaller lesions this has usually comprised simply placing a piece of gauze or similar material against the wound and then removing it some time after bleeding has stopped. In this case the only hemostatic agent is in the blood itself.

The present invention consists of an improved surgical dressing which comprises in combination a fibrous material and a water insoluble alginic material. At the same time, the combination may also include antibacterial agents stable in an acid or slightly alkaline medium.

More specifically, the invention may be applied to a surgical dressing for topical application wherein an adhesive coated backing is covered in part with a fibrous material, such as gauze, at least the surface layer of which contains alginic acid. This will preferably also contain an antibacterial agent such as tyrothricin. As will be shown below, the alginic acid while present in relatively large quantities does not reduce the antibacterial effect of the tyrothricin and at the same time very substantially increases the hemostatic effect of the surgical dressing. In addition steam sterilisation does not adversely affect either the hemostatic or antibacterial activity of the material.

The water insoluble alginic material includes alginic acid itself which may be substantially pure or which may contain small amounts of metallic alginate, and particularly of the insoluble type such as calcium alginate. Small amounts of calcium as, for example, up to 3% by weight, may be advantageous in further stabilising the alginic material in sterilisation. Alternatively, the alginic acid may be in an oxidised form and it may be combined with a small amount of a dilute solution of strong mineral acid, such as nitric acid. The alginic material may be in the form of a gel or a gauze, but will preferably be in the form of finely divided particles which prior to application constitute a powder. Alternatively the alginic acid may be in the form of fibres which may be blended with the cotton or other fibrous material.

The useful antibacterial materials (i.e. materials which either destroy or inhibit harmful bacteria) are those which are stable in acid or slightly alkaline medium such as sulfa drugs and tyrothricin. The latter has been found to be particularly adaptable both as being compatible with the alginic material as well as withstanding steam sterilisation.

Tyrothricin is a known water-insoluble, alcohol-soluble substance, extracted from cultures of an aerobic spore-forming soil bacillus, Bacillus brevis. It is a powder which can be separated into two crystalline components, gramicidin and

tyrocidine. The gramicidin may be, for example, from 10 to 25 per cent, and the tyrocidine from 40 to 60 per cent. It is known that tyrothricin is bactericidal *in vivo* to a large number of Gram-positive bacteria and bacteriostatic to many other bacteria, this action being due to the gramicidine component, since tyrocidine is inactivated by the tissue fluids of the body. Because tyrothricin is insoluble in water, the tyrothricin powder cannot be applied effectively to wounds in dry form for it is not taken up by the body fluids but remains inert in the wound. Hence it has been customary to apply throthricin to wounds in alcoholic solutions or dilute alcoholic dispersions.

A particularly effective and non-toxic solution of tyrothricin (containing about 20% gramicidin) for the antibacterial treatment of wounds and ulcers is a concentration of about 500 micrograms per cc., which kills a wide range of bacteria and prevents the growth of many others. Stronger or weaker concentrations may be used in particular circumstances, for example, from 100 to 1000 micrograms per cc. It is also known that very large dosages or concentrations may be toxic especially in body cavities, such as the peritoneal cavity. As concentrations increase above about 1000 micrograms per cc., no important increase in antibacterial activity occurs, while the toxicity to tissues begins to increase. On the other hand concentrations below 1000 micrograms per cc. are not toxic, but antibacterial activity with respect to certain organisms begins to diminish in concentrations much below 500 micrograms per cc. Consequently the preferred concentrations are between about 500 and 1000.

Since the antibacterial activity of tyrothricin in the body is due to the gramicidin content (the tyrocidine being inactivated by the tissue fluids) gramicidin itself can be used to impregnate the dressings, adjusting the quantity to the proportion of gramicidin in the tyrothricin, as noted above. However, tyrothricin is preferable because of its ready availability and adequate antibacterial activity; moreover, the tyrocidine component, although not active against bacteria in the body, is nevertheless beneficial because it helps solubilise the gramicidin component and because it is a surface tension depressant or wetting agent, which helps the solution penetrate the wound and thus reach bacteria beneath the surface. It is known that some antibacterial agents do not act beneath the surface.

Propylene glycol may be used as the solvent for the tyrothricin or any non-toxic non-volatile (at ordinary sterilisation temperature) solvent which is miscible with body fluids. For example:—

Dipropylene glycol
Glycerol
Arlex (Registered Trade Mark) (85% Sorbitol)
Ethylene glycol
Diethylene glycol
Triethylene glycol
Polyethylene glycol 200
Polyethylene glycol 300
Polyethylene glycol 400
Polyethylene glycol 600
Carbowax 1000
Carbowax 6000
Cellosolve (Registered Trade Mark)
Methyl cellosolve
Methyl cellosolve acetate
Monoethanolamine
Diethanolamine
Triethanolamine
Morpholine

The amount of solvent used should be just sufficient so that the finished dressing is dry to the touch.

The fibrous material with which the alginic material and antibacterial are combined may be any of a number of fibrous materials, such as paper or textiles and may include any type of cloth or loose fibres such as raw cotton, but will preferably be combined with cotton gauze.

In general, the material to be impregnated, such as gauze, will be passed through a solution containing both the alginic material and antibacterial. However, other methods of impregnation or coating may be used, such as separate impregnation with the antibacterial and with the alginic material or the water-insoluble alginic material may be produced on the fibres themselves by first impregnating the fibres with a water soluble alginic material and subsequently precipitating a water insoluble alginic material *in situ*.

After impregnation the fibrous material is dried at an elevated temperature. It may not at this time contain sufficient of the alginic material and it may be impregnated and dried again, such that from about 10 to about 75 per cent by weight based on the weight of the fibre is alginic material and preferably between 30 and 40 per cent.

The dried fibrous material containing the alginic material and the antibacterial are preferably sterilised and this may be done in any of a number of ways, such as, for example, formaldehyde vapour or steam sterilisation, but the latter is preferable and this may be done after the material is packaged.

In a preferred form the surgical dress-

ing comprises, as is illustrated in the accompanying perspective drawing, a normally tacky pressure sensitive adhesive strip 10 carrying a suitable resilient absorbent compress pad 11 of surgical gauze the outer layer 12 of which is impregnated with alginic acid and tyrothricin in ethylene glycol.

EXAMPLE

0.7570 parts of tyrothricin were mixed with 40 parts of propylene glycol and 160 parts of water. A mechanical agitator was used to get the tyrothricin in solution. Separately 50 parts of alginic acid was dissolved in 412 parts of water by the addition of 18 parts of 28% ammonium hydroxide. After all the alginic acid was in solution, it was filtered through a gauze filter to take out any siliceous impurities. To this solution was added 20 parts of tyrothricin solution prepared above. The combined solution was allowed to stand for several hours and then a strip of cotton gauze was immersed in the combined solution for a few minutes, put through a squeeze roller, and dried in an oven at 70° C. After drying the gauze was again immersed in the combined solution, squeezed, and dried a second, third and fourth time, until the material picked up by the gauze constituted 61.2 per cent by weight on a dry basis of the total material.

A small strip of the gauze thus treated was then secured to a strip of adhesive tape and two layers of untreated gauze placed between the outer layer of treated gauze and the adhesive tape backing. This bandage was placed upon a bleeding surface cut and found to give excellent hemostatic results.

The following table shows results of assay test for bacteriological activity on samples of alginic acid tyrothricin impregnated gauzes. The results in the table are obtained by a test method which comprised a culture of Lancefield hemolytic streptococcus covering agar petri dishes upon which were placed the gauze samples and the results indicate the clear areas found on the dishes after 18 hours incubation.

TABLE I.

Per Cent Alginic Acid	Per Cent Propylene Glycol	Tyrothricin	Clear Zone	Semi-clear Zone
43.48	17.39	15.6 micrograms/sq.cm.	2.0 mm.	1.8 mm.
46.52	13.29	8.75	2.0 mm.	2.5 mm.
44.38	17.75	12.65	2.0 mm.	4.0 mm.
0	—	8.7	2.0 mm.	4.0 mm.
37.6	0	0	0	0

It will be seen from this table that the alginic acid has little or no effect upon the antibacterial action of the tyrothricin and that the amount of tyrothricin is not critical within reasonable limits.

The following table illustrates the hemostatic effect of alginic acid coated gauze as compared with a control of untreated gauze. Tests on animals utilised a pierced femoral vein technique. Time given is that required to stop bleeding.

TABLE II.

Sample	Per Cent Alginic Acid	Animal	Impregnated Gauze	Plain Gauze
1	20.22	A	3 min. 15 sec.	7 min.
		B	1 min. 45 sec.	3 min.
2	10.81	C	2 min. 20 sec.	4 min. 30 sec.
		D	3 min.	3 min. 20 sec.
3	26.09	E	2 min 40 sec.	4 min. 30 sec.
		F	1 min. 30 sec.	1 min. 40 sec.
4	35.95	G	1 min. 10 sec.	5 min. 10 sec.
		H	1 min. 50 sec.	4 min.

It will be seen from this table that the alginic acid impregnated gauze is very effective in reducing the time required to stop bleeding.

It may be mentioned that our co-pending Specification No. 15443/47 (Serial No. 627,797) describes and claims a surgical dressing having a high antibacterial activity in the presence of body tissue fluids comprising a fibrous carrier having deposited thereon a solution containing gramicidin in a non-volatile solvent miscible with body tissue fluids, said dressing being dry to the touch.

Having now particularly described and ascertained the nature of our said invention and in what manner the same is to be performed, we declare that what we claim is:—

1. A surgical dressing having improved

hemostatic properties comprising a fibrous carrier and a water-insoluble alginic material carried thereby.

2. A surgical dressing having improved hemostatic properties comprising cotton gauze and a water-insoluble alginic material carried thereby.

3. A surgical dressing as claimed in claim 1 or 2 in which the fibrous carrier or cotton gauze is impregnated with alginic acid.

4. A surgical dressing as claimed in any of claims 1—3 in which the fibrous carrier also carries an antibacterial which is stable in an acid or slightly alkaline medium.

5. A surgical dressing as claimed in claim 4 in which the antibacterial is gramicidin or tyrothricin.

6. A surgical dressing as claimed in claim 5 in which the fibrous carrier has on its surface a water-insoluble alginic material and tyrothricin in a solution of ethylene glycol, the dressing being dry to the touch.

7. A surgical dressing as claimed in claim 6 in which 500—1000 micrograms of tyrothricin are employed per cc. of ethylene glycol.

8. An adhesive compress dressing having improved hemostatic properties comprising in combination a normally tacky pressure sensitive adhesive strip, a resilient pad secured to said strip and a hemostatic covering on said pad, said covering comprising a fibrous material impregnated with a water-insoluble alginic material.

9. An adhesive compress dressing as claimed in claim 8 in which the fibrous material is impregnated with alginic acid and tyrothricin dissolved in a non-volatile solvent miscible with body fluids, said pad being dry to the touch.

10. A method of making a surgical dressing having improved hemostatic properties comprising impregnating a fibrous carrier with a solution comprising a water-insoluble alginic material in a solution of ammonium hydroxide, drying the impregnated fibrous material, and sterilising the dressing by exposure to temperatures above the boiling point of water.

11. The dressing or the method of making the same, as claimed in any of the preceding claims, in which there is employed 30 to 40 per cent by weight based on the fibrous carrier, of the water-insoluble alginic material.

12. The dressing or the method of making the same, as claimed in any of the preceding claims in which the alginic material is combined with a small amount of a dilute solution of a strong mineral acid.

13. The dressing or the method of making the same, as claimed in claim 12, in which the acid is nitric acid.

14. The manufacture of a surgical dressing substantially as described in the Example.

Dated this 13th day of June, 1947.
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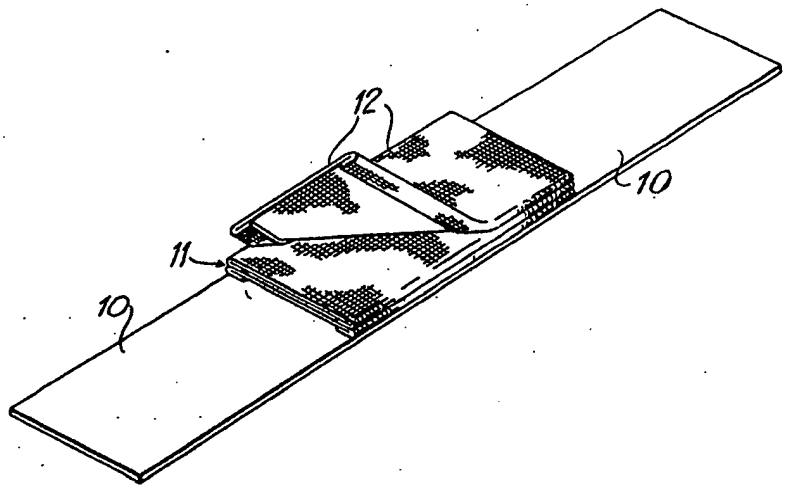

[This Drawing is a reproduction of the Original on a reduced scale.]

H.M.S.O.(Ty. P.)